

Amendments to the Claims:

This listing of the claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1 (Currently Amended). A method for monitoring the effectiveness of an administered agent that interacts with the A₃ adenosine receptor (A3AR) in a treatment of a disease state in an individual, the method comprising

- (i) at a defined time point following administration of the agent to the individual, selected such so as to permit the agent to reach and affect cells in the individual that are associated with the disease state, withdrawing a sample of said cells or tissue containing said cells from the individual;
- (ii) detecting the level of at least one physiological parameter of at least one biological marker in said cells, the marker being an A3AR, or an element associated with the A3AR signal ~~transduction~~ transduction pathway downstream to A3AR; and
- (iii) comparing the level of said at least one parameter to a control level, being the level thereof in such cells or tissue from the same

individual before administration of said agent,
or being a standard reference for said marker
which is indicative of a ~~n-un-treated~~ an
untreated disease state;

wherein a difference in level of the physiological parameter
from control ~~being~~ is indicative of the effectiveness of said
treatment against ~~these~~ the disease state.

2 (Currently Amended). The method according to
claim 1, wherein the agent that interacts with the A3AR is an
A3AR agonist.

3 (Currently Amended). A method according to claim
1, wherein the A3AR signal transduction pathway is the Wnt
pathway.

4 (Currently Amended). A method according to claim
3, wherein the element is at least one element selected from
the group consisting of PKA, PKB/Akt, GSK-3 β , β -catenin,
cyclin D1, and c-myc.

5 (Currently Amended). A method according to claim
1, wherein the A3AR signal transduction pathway is the NF- κ B
pathway.

6 (Currently Amended). A method according to claim
5, wherein the element is at least one element selected from
the group consisting of NF- κ B, PI3K, IKK, c-myc, and cyclin
D1.

7 (Currently Amended). A method according to claim 1, wherein the physiological parameter is selected from the group consisting of the level of mRNA or protein expression, the level of phosphorylation, and the cellular localization.

8 (Original). The method of claim 1, wherein said disease state is a proliferative-related disease.

9 (Original). The method of claim 8, wherein said disease is cancer.

10 (Original). The method of claim 9, wherein said cancer is melanoma, colon carcinoma or prostate cancer.

11 (Original). The method of claim 8, wherein said disease is an inflammatory disease.

12 (Currently Amended). The method according to claim 8, wherein effective treatment against the disease is indicated by a change in a physiological parameter of a biological marker selected from the group consisting of:

- (a) a decrease of the protein level or the mRNA level coding ~~therefore-therfor,~~ of at least one of A3AR, PKB/Akt, PKA, β -catenin, c-myc, cyclin D1, ~~and~~ NF- κ B, and TNF- α ; or an increase in the protein level or mRNA coding ~~therefore-therfor~~ of GSK-3 β ;
- (b) at least one change in phosphorylation level selected from the group consisting of a

decrease in phosphorylation level of ~~GSK-3 β~~
~~GSK-3 β~~ , and an increase in the phosphorylation
level of PKB/Akt, PKA or β -catenin~~;~~; and

- (c) at least one change in cellular localization
selected from the group consisting of: a
decrease in the localization of A3AR receptor
in the cellular membrane as compared to
control, and a decrease in the localization of
 β -catenin or NF- κ B in the nucleus as compared
to cytosol.

13 (Currently Amended). A method according to claim
1, wherein said disease state is a disease or condition
wherein a beneficial therapeutic effect is evident by
increased proliferation.

14 (Currently Amended). The method of claim 13,
wherein said disease state is a decrease in white blood cell
count, especially neutrophils, as a result of chemo- or radio-
therapy.

15 (Currently Amended). The method of claim 13,
wherein effective treatment against the disease is indicated
by a change in a physiological parameter of a biological
marker selected from the group consisting of:

- (a) an increase of the protein level, or of the
level of mRNA coding ~~therefor~~ therefor, of at

least one of A3AR, PKB/Akt, PKA, β -catenin, c-myc, cyclin D1 and NF- κ B, or a decrease in the protein or mRNA level of GSK-3 β ;

(b) at least one change in phosphorylation level selected from the group consisting of+ an increase in phosphorylation level of GSK-3 β , and a decrease in the phosphorylation level of PKB/Akt, PKA or ~~in the phosphorylation level of~~ β -catenin; and

(c) at least one change in cellular localization selected from the group consisting of+ an increase in the localization of A3AR receptor in the cellular membrane as compared to control, and an increase in the localization of β -catenin in the nucleus as compared to cytosol.

16 (Currently Amended). A method according to claim 1, wherein the level of the at least one physiological parameter of the at ~~least~~least one biological marker is determined at a time point after the administration of the agent, wherein the differences between the level of the parameter in the treated subject and the untreated control are expected to be the most prominent.

17 (Currently Amended). A method according to claim 2, wherein the A3AR agonist is 1-deoxy-1-[6[[3-iodophenyl)methyl]amino]-9H-purine-9-yl]-N-methyl- β -D-ribofura-nuronaminde (IB-MECA).

18-24 (Canceled).

25 (Currently Amended). A method for determining whether a drug candidate is an A3AR agonist useful in treating a disease state manifested in diseased cells, the method comprising:

- (i) administering said drug candidate to a subject having said disease state;
- (ii) at one or more defined time points following the administration, withdrawing a sample of the diseased cells or tissue containing said cells from the subject;
- (iii) detecting the level of at least one physiological parameter of at least one biological marker in said cells, the marker being an A3AR, or an element associated with the A3AR signal ~~transudation~~ transduction pathway which is downstream to the A3AR; and
- (iv) comparing the level of said at least one parameter to the level in diseased cells

withdrawn from a subject not administered with
said drug candidate;

wherein a difference in level of the physiological parameter
between the treated and untreated sample ~~being~~is indicative
that the drug candidate is an agonist of A3AR.

26 (Currently Amended). A method according to claim
25, wherein the A3AR signal transduction pathway is the Wnt
pathway.

27 (Currently Amended). A method according to claim
26, wherein the element is at least one element selected from
the group consisting of+ PKA, PKB/Akt, GSK-3 β , β -catenin,
cyclin D1, and c-myc.

28 (Currently Amended). A method according to claim
25, wherein the A3AR signal transduction pathway is the NF- κ B
pathway.

29 (Currently Amended). A method according to claim
22, wherein the element is at least one element selected from
the group consisting of+ NF- κ B, PI3K, IKK, TNF- α , c-myc, and
cyclin D1.

30 (Currently Amended). A method according to claim
25 wherein the physiological parameter is selected from the
group consisting of+ the level of mRNA or protein expression,
the level of phosphorylation, and the cellular localization.

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31 (Currently Amended). The method of claim 25,
wherein said disease state is a proliferative-related disease.